In the Sequence Listing:

Please insert the attached paper copy of the Sequence Listing as new pages 1-3 in the above-captioned application. A computer-readable form (CRF) copy of the Sequence Listing accompanies this response.

AMENDMENT

In the Specification:

Please replace paragraph [0133] with the following rewritten paragraph [0133]:

--*Construction of plasmids pRSG32, pBP49, pRSG50*: Genes encoding DEBS1+TE (pRSG32), DEBS2 (pBP49) and DEBS3 (pRSG50) were cloned into pET21c (Novagen). The DEBS1+TE gene was cloned as the *Nde*I-*Eco*RI fragment from pCK12 (6). The DEBS3 gene was cloned as the *Nde*I-*Eco*RI fragment from pJRJ10 (Jacobsen, J. R., *et al., Biochemistry* (1998) 37:4928). To express the DEBS2 gene, the *Bsm*I-*Eco*RI fragment from pRSG34 (Gokhale, R. S., *et al., Science* (1999) 284:482), which has been used previously to express module 3+TE, was replaced with a *Bsm*I-*Eco*RI fragment encoding module 4. The *Eco*RI site (in bold) was engineered immediately upstream of the stop codon of the DEBS2 gene by modifying the natural sequence to the following: CGGGGGAGAGGACCT**GAATTC** (SEQ ID NO: 1)--

Please replace paragraph [0156] with the following rewritten paragraph [0156]:

--*Construction of plasmids pBP130, pBP144:* The expression vectors pET21c and pET28a were first re-engineered by replacing the Bpu1102I-DraIII fragments in these vectors with a polylinker possessing the Bpu1102I, NsiI, PstI, PacI and DraIII sites. The DEBS2 gene from pBP49 and the DEBS3 gene from pRSG50 were cloned into the pET21c derivative between the NdeI-EcoRI and NsiI-PacI sites, respectively, yielding pBP130 (25.5 kb). Thus, pBP130 is capable of expressing the DEBS2 and DEBS3 genes under the control of the same pT7 promoter. Similarly, pBP144 (20 kb) was constructed from the pET28a derivative described

above by inserting the *pccAB* genes from pTR132 (Rodriguez, E., and Gramajo, H., *Microbiology* (1999) 145:3109-3119) and the DEBS1 gene into the NdeI-EcoRI and PstI-PacI sites, respectively. This DEBS1 gene was derived from pRSG32 by replacing the SpeI-EcoRI fragment with a fragment amplified from the 3' end of the natural DEBS1 gene using the following oligonucleotides: 5' oligonucleotide: TTACTAGTGAGCTCGGCACCGAGGTCCGGGG (SEQ ID NO: 2); 3' oligonucleotide: TTGAATTCGGATCGCCGTCGAGCTCCCGGCCGA (SEQ ID NO: 3). Thus, pBP144 expresses the *pccAB* genes and the DEBS1 gene, each under the control of its own pT7 promoter.--

Please replace paragraph [0166] with the following rewritten paragraph [0166]:

--*Construction of an Expression Vector for the A-T Didomain.* An NdeI restriction site was engineered at the start codon of the *rifA* gene using the primers 5'-GCGGC**CATATG**CGCACCGATCTC-3' (SEQ ID NO: 4) and 5'-AGGGCCCGCTGGCGGGAGAAC-3' (SEQ ID NO: 5) (mutated bases are shown in bold, and the introduced NdeI restriction site is underlined); the amplified 2.5 kb fragment was ligated to linearized pCR-Script (Stratagene) to produce pHu29. The *rifA* gene with the engineered NdeI restriction site at the start codon was then reconstructed in pHu90-1, a derivative of pRM5 (McDaniel, R., et al. (1993) Science 262, 1546-1550), via pHu29, pHu35, pHu50, and pHu51. Flanking restriction sites for PacI and PstI were used to transfer the sequence encoding the loading didomain and part of module 1 from pHu90-1 into a pUC18 derivative to produce pSA2. The loading didomain and module 1 are separated by an ~20 amino acid linker region, delineated by the C-terminal end of the consensus T domain of the loading didomain and the N-terminal end of the consensus ketosynthase domain of module 1 (GenBank accession no. AF040570). To isolate the loading didomain from module 1, a NotI restriction site was introduced into the linker sequence using the primers 5'-ACCGAGACCTGCGGGGCGATCA-3' (SEQ ID NO: 6) and 5'-**GCGG**CCGCGACGGCCTGCGTG-3' (SEQ ID NO: 7) (mutated bases are shown in bold,

and the introduced NotI restriction site is underlined); the resulting 0.94 kb fragment encodes from within the loading didomain into the linker region. This amplified fragment was ligated to linearized pCR-Blunt (Invitrogen) to produce pSA4, which was then digested with BamHI and PstI and ligated to pSA2 digested with the same enzymes to generate pSA6. The 1.9 kb NdeI–NotI fragment derived from pSA6 was ligated to NdeI–NotI-digested pET21c (Novagen) to produce pSA8, an expression vector for the loading didomain with hexahistidine appended to its C-terminus.--

Please replace paragraph [0186] with the following rewritten paragraph [0186]:

--To engineer a functional fusion between the A-T loading didomain from the rifamycin synthetase and the first module of DEBS, the DNA sequence immediately upstream of the KS domain in DEBS module 1 was modified to read as follows: CCGGCGAACC**GAT**CGCG**ATC**GTCGCGATGG (SEQ ID NO: 8). The engineered BsaBI site (in bold) was fused to the corresponding naturally occurring BsaBI site between the A-T loading didomain and the first PKS module of the rifamycin synthetase (Figure 6). The resulting fusion was transferred into pBP144 in place of DEBS1, giving rise to pBP165.--